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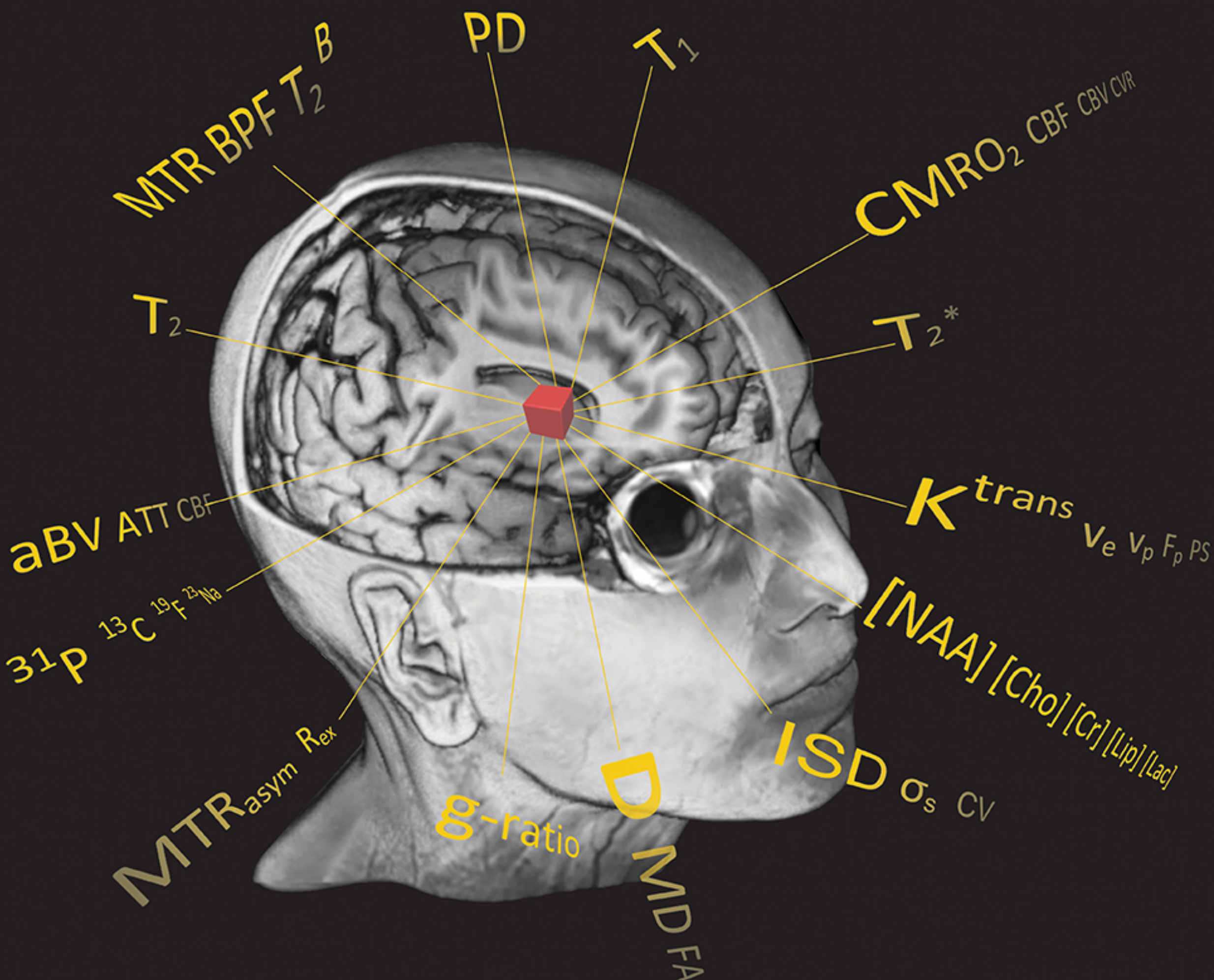

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Nicholas G. Dowell
Paul S. Tofts

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Quantitative MRI of the Brain

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Foreword

It is remarkable how much progress has occurred since the publication of Paul S. Tofts' first edition in 2003. Remember that radiology began as a highly qualitative field where shapes and patterns were correlated with diseases. Initially, magnetic resonance imaging thrived because it could produce undistorted views in three planes. It has evolved considerably from beautiful images to being able to truly predict *in vivo* pathology. The previous edition of this book was ahead of its time in articulating the vision of quantitative MRI. How far the field will go in the future depends on the creativity of investigators and their ability to understand and solve technical problems.

To reliably predict biology on combinations of techniques could change approaches to disease. There are indeed many possibilities for the future including accuracy in differentiating aspects of disease such as tumor versus edema, necrosis versus tumor, benign versus malignant, and the grail – biological aggressiveness of lesions. The opportunities are abundant. I will cite two examples. Think about being able to predict aggressiveness and tumor volume of prostate cancer – totally changing how surveillance is carried out. MR may also be able to accurately separate therapeutic tissue changes such as the effects of radiation or immunotherapy from recurrent tumor. This is essential in detecting infiltrating neoplasms such as glioma.

For those engaged in imaging, understanding how physical principles can be applied to produce quantitative results has the prospect of transforming communications, monitoring, and reporting. It is the path where MR and medicine are heading. Quantitation provides objective measures of activity and disease – vital to assessing the extent of pathology and determining the success of particular treatment protocols. The power of quantitative MR is underscored today by its incorporation in clinical trials to demonstrate efficacy.

Quantitative MRI of the Brain begins with basic discussion of data collection and image generation. Chapter 3 discusses quality assurance, precision, and accuracy. These concepts are critical to consistency, an essential element of quantitative imaging. Once grounded in the essentials of reproducibility, the text leads the reader through relaxation times and biophysical principles of susceptibility, diffusion, and magnetisation transfer. The last chapters focus on techniques including functional MRI, spectroscopy, and perfusion.

Paul S. Tofts and his co-editors, Mara Cercignani and Nicholas G. Dowell, have done a magnificent job assembling contributors with appropriate expertise and have been successful in compiling the requisites necessary to achieve a high level of understanding in quantitative MR. This is not a small feat and is necessary for advancing the field. Congratulations on a significant accomplishment!

Robert I. Grossman
NYU Langone Health

Foreword to the First Edition

Paul S. Tofts has succeeded brilliantly in capturing the essence of what needs to become the future of radiology in particular, and medicine in general – quantitative measurements of disease. This is a critical notion. The discipline of radiology started with the ability to discern the shadows that were abnormal. On chest x-rays, one could see the 'white in the right' and that was correlated to the clinical diagnosis of pneumonia. It is truly amazing how long such descriptions were adequate and indeed, the state of the art. This transcended the modern era of cross-sectional imaging. CT and then MR heralded the ability to not only observe pathological states but to specifically define and locate such conditions. Based upon absorption of biophysical parameters combined with position, one could suggest that a particular abnormality was a stroke rather than a tumour or an infection. Make no mistake about it, this was an incredible scientific leap and has totally changed the calculus of medicine. In the twenty-first century radiologists have become both the diagnostician and the arbiter of therapeutic efficacy. In clinical neuroscience the function of the neurologic exam has been diminished by the unbiased, reliable nature of imaging. This has been mirrored throughout the body. The preeminent role of imaging now requires a new level of metric-quantitative measurements.

Why is quantitative methodology so vital? First and foremost, it is relatively unbiased compared with qualitative descriptions. Second, it lends itself easily to statistical modelling. Lastly, if performed correctly, the data can be pooled over multiple centres to provide power regarding a clinical trial or longitudinal study. Thus, the natural history of a disease such as multiple sclerosis may be ascertained by a time-dependent study. This was first made apparent when the FDA in the United States approved the use of interferon beta-1b in 1993 based upon MRI data that revealed a decrease in disease activity and lesion burden. The effect of the drug could not be ascertained from the clinical measure of disability, the acknowledged gold standard for multiple sclerosis. Approval of interferon beta changed the course of clinical treatment trials. What has ensued is a discussion of surrogate markers in imaging, sensitivity, specificity, reproducibility, etc. The bottom line is the emergence of the mandatory need to incorporate quantitative imaging techniques into treatment trails.

This book addresses the measurement process, the measures, what the measures mean biologically, and image analysis methodology. Any physician/scientist participating in a scientific study or clinical trial must be familiar with the concepts elucidated in this book. Although the text is focused on the brain, the concepts pertain to any imaging study. How to ensure that your results will stand the test of the critical review is the underlying theme of the first section on the concept of measurement in MR. Thorough knowledge of the principles of accuracy, precision, and quality assurance are essential to the writing of any imaging proposal and the subsequent performance of the study.

The second section is focused on the metrics themselves. Here, there are lucid discussions of MR parameters that are the windows on the pathological processes we wish to study. This is complete and covers the intrinsic MR parameters (T_1, T_2, PD), diffusion, magnetisation, transfer, spectroscopy, dynamic contrast, perfusion, and fMRI. To appreciate the strengths and limitations of these measures enables the reader to identify optimal parameters for particular studies. It also assists in the interpretation of the current literature. The section offers a complete survey of all of the metrics used in clinical MR today.

The chapter on the biological significance of the MR parameters in multiple sclerosis translates the imaging parameters to their biological correlates. This is important, for if the measures are just abstract it is hard to argue for their implementation.

The last major section of the book deals with the topics of registration of images and other measures, including atrophy, texture, and volumetric analysis. Image registration is fundamental when performing any longitudinal analysis. Just think about it. When a radiologist is asked if a lesion has changed on two different studies, one must be careful that the apparent change is not the result of technical differences (slice alignment, slice thickness, etc.).

I was honoured to be asked by Professor Tofts to write this foreword. In my opinion this text is a beautifully executed work, capturing what is essential for radiologists and scientists to understand about quantitative MR measures. There is no more qualified individual up to this task than Dr. Tofts. He is a lucid and most thoughtful scientist. I wish to extend my congratulations to him and the other authors on this effort. This book will become a classic and the first of many on this significant topic.

Robert I. Grossman
New York University School of Medicine

Editors

Mara Cercignani is professor of Medical Physics at the Brighton and Sussex Medical School (BSMS). She has worked in the field of MRI since 1998, and received her Doctorate from University College London in 2007. Before moving to BSMS in 2011, she worked at San Raffaele Hospital in Milan (1998–2002), the Institute of Neurology in London (2002–2007) and Santa Lucia Foundation in Rome (2007–2011). Her main research interests lie with the field of quantitative MRI, spanning from diffusion MRI to quantitative magnetisation transfer imaging.

Nicholas G. Dowell is a lecturer in Imaging Physics at the Brighton and Sussex Medical School (BSMS). He received his Doctorate in solid-state nuclear magnetic resonance from the University of Exeter in 2004 before moving to the Institute of Neurology, University College London, to work on quantitative magnetic resonance imaging. He moved to the newly opened Clinical Imaging Sciences Centre at BSMS in 2007. His research interests lie principally with quantitative magnetisation transfer, diffusion-weighted imaging, data modelling and analysis techniques in the brain.

Paul S. Tofts is emeritus professor at the Brighton and Sussex Medical School (BSMS). After obtaining a BA in Physics from Oxford University in 1970, the new University of Sussex provided an ideal contrasting environment where his D Phil was in experimental NMR studies of helium at low temperature. When biomedical NMR hardly existed, from 1975 he researched radioisotope and CT imaging at the Royal Postgraduate Medical School, London. At University College London, in 1978, he developed a prototype ^{31}P NMR machine for newborn babies and started a career in quantitative MR with the first measurement of absolute metabolite concentrations *in vivo*.

An early MRI machine in 1985 devoted to multiple sclerosis studies at the Institute of Neurology, Queen Square (now part of University College London), enabled Paul to develop a whole range of quantitative imaging techniques and to edit the first book on quantitative MRI. Analysis of dynamic Gd-enhanced image data enabled the quantifying of blood–brain barrier leakage, and his mathematical model is now used extensively.

The new imaging centre at BSMS attracted Paul to return in 2006 to Sussex as the foundation chair of Imaging Physics until 2009. He has 215 publications, 15,000 citations and an h-factor of 62.

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